

REMARKS

Review and reconsideration of the final Office Action mailed November 9, 2011 (hereinafter "Office Action"), is respectfully requested in view of the arguments made herein. Because this Amendment is being filed within two months of the date the Office Action was mailed, Applicant respectfully requests the benefits of the extension to time provisions set forth on pages 8-9 of the Office Action. No fees are believed due; however, the Commissioner is hereby authorized to charge any deficiency or credit any surplus to Deposit Account No. 04-1679.

In the Office Action, claims 36-48 were pending, with claims 36-42, 44-46 and 48 being drawn to an elected invention. Claims 36-42, 44-46 and 48 stand rejected under 35 U.S.C. §103(a).

**Claim Rejections – 35 USC §103(a)**

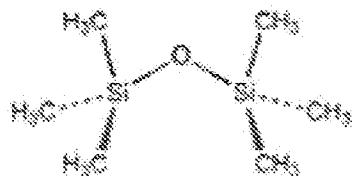
In the Office Action, claims 36-42, 45, 46 and 48 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 7,820,284 by Terry ("Terry") in view of U.S. Patent No. 7,157,145 by Vissing et al. ("Vissing"); and Claim 44 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Terry in view of Vissing et al. as applied to claims 36-42, 45 and 46, and further in view of U.S. Patent No. 6,333,093 by Burrell et al. ("Burrell").

**General Overview of Plasma Polymer Formation Process**

The Office Action includes arguments that the compositions in Vissing and the Specification are the same and would therefore have the same properties. In particular, "The Examiner notes that the same polymer, hexamethyldisiloxane, is used by Applicant in their disclosed examples as their transport layer (see Example 1, for instance) wherein it's stated that the antimicrobial layer is 'coated with a hydrophilic plasma polymer (transport control layer).'" The Examiner then indicates concerns that it appears "Applicant is alleging that the polymers of

Vissing are hydrophobic while simultaneously using the very same plasma polymers of Vissing and describing it as hydrophilic." Office Action, Page 3.

As an initial matter, Applicant notes that hexamethyldisiloxane is a monomer, not a polymer. For convenience, the chemical structure of hexamethyldisiloxane is shown below:



It should also be noted that hexamethyldisiloxane is a precursor to the plasma polymerization process, not the polymeric product formed by a plasma polymerization process. See, e.g., Specification, Example 1, page 15, line 15; and Vissing, Example 1, column 5, lines 40-42 and Example 2, column 6, lines 31-33. Both the Specification and Vissing include examples where the polymer is formed from oxygen and hexamethyldisiloxane (HMDSO) using a plasma polymerization process. *Id.* Thus, it should be understood that plasma polymerization utilizes a plasma (*i.e.*, the ionized gaseous state) to form polymers from low molecular weight precursors like HMDSO.

While the same precursors may be used (*e.g.*, HMDSO and O<sub>2</sub>), it is critical to understand that the structure and composition of the polymer formed using plasma polymerization depends on the structure of the ionic fragments formed in the plasma state. The structure of these fragments depends not only on the particular precursors and the ratios thereof but also on numerous other variables (power, pressure, duration, presence and concentration of the precursors and other reactive gases, such as hydrogen) of plasma formation. Thus, depending on the variables utilized in the plasma polymerization process, the "same" precursor (*e.g.*, HMDSO) can be used to form plasma polymer layers having a wide range of different compositions and properties (*e.g.*, hydrophilic v. hydrophobic properties).

A significant factor that influences the hydrophilic/hydrophobic characteristics of a plasma polymer layer obtained using HMDSO is the ratio of oxygen-to-HMDSO in the plasma feed stream.

See, e.g., Specification, Page 6, Lines 14-27. A high relative concentration of oxygen in the plasma feed results in a large number of oxygen-containing functional groups (e.g., hydroxy -OH, carbonyl C=O, silanol -Si-OH, siloxane -Si-O-Si-) in the resulting polymer material. Because such functional groups impart hydrophilicity to the resulting polymer, the formed polymer is generally more hydrophilic where the number of oxygen-containing functional groups is higher. In addition, a larger number of oxygen-containing functional groups corresponds to a higher ratio of oxygen-to-carbon and oxygen-to-silicon in the plasma polymer. The ratio of oxygen-to-carbon and oxygen-to-silicon is higher where more oxygen is present upon plasma polymerization.

The plasma polymer layer is also more hydrophobic when the amount of carbon is increased because the higher the carbon content the more organic (hydrocarbon-like) the character of the polymer. The higher the oxygen content of the plasma gas, the more of the carbon of the precursor is oxidized to CO<sub>2</sub>, thus resulting in a lower carbon content and accordingly stronger hydrophilic characteristics of the plasma polymer.

In summary, where the polymer is produced from a feed stream including HMDSO and O<sub>2</sub>, the higher the relative amount of O<sub>2</sub> present in the plasma feed stream, the more hydrophilic the resulting polymer. In addition, the resulting polymers are more hydrophilic where the ratio of C:Si is lower and where the ratio of O:Si is lower. Applicant hopes that this overview helps clarify the Arguments made herein.

Comments and Remarks

Applicant now turn to the rejections at hand. As set forth in claim 36, the claimed layered material is drawn to:

36. (Previously presented) A layered material, comprising:
  - a) a biocide layer having a biocidal active agent, and
  - b) a transport control layer covering the biocide layer, having a thickness and porosity adjusted to release an antimicrobial and non-cytotoxic quantity of the biocidal active agent out of the biocide layer and through the transport control layer, wherein the transport control layer is a plasma polymer

layer and/or a sputter-applied layer and wherein the transport control layer has a silicon content of 20 to 60%, a carbon content of 10 to 30%, and an oxygen content of 30 to 50%.

The claimed layered material include a biocide layer having a biocidal active agent, and a transport control layer covering the biocide layer. *Of particular interest, the transport control layer has a thickness and porosity adjusted to release an antimicrobial and non-cytotoxic quantity of the biocidal active agent out of the biocide layer and through the transport control layer.* The transport control layer has a silicon content of 20 to 60%, a carbon content of 10 to 30%, and an oxygen content of 30 to 50%, and is formed by as a plasma polymer layer and/or a sputter-applied layer.

As explained above, where a polymer is produced from a feed stream including HMDSO and O<sub>2</sub>, the higher the relative amount of O<sub>2</sub> present in the plasma feed stream, the more hydrophilic the resulting polymer. In addition, the resulting polymers are more hydrophilic where the ratio of C:Si is lower and where the ratio of O:Si is lower. Applicant hopes that this overview helps clarify the Arguments made herein.

Specific Examples of Hydrophilic and Hydrophobic Plasma Polymers

According to Example 1 of the present application, a plasma polymer layer produced using hexamethyldisiloxane (HMDSO) as precursor is applied. The plasma polymerization is performed under an operating pressure of 0.07 mbar with an operating gas comprised of 95 % O<sub>2</sub> and 5 % HMDSO. After 45 seconds of plasma polymerisation performed under said conditions, the silver layer is coated with a hydrophilic plasma polymer (transport control layer) with a thickness of 45 nm. Specification, Page 15, lines 18-24.

The chemical composition of this plasma polymer is disclosed in Example 4 of the present application. According to XPS analysis, the surface of the transport control layer has a an oxygen content of 39.4 atomic %, a carbon content of 24 atomic % and silicon content of 36.6 atomic %

(according to page 12, lines 5-6, the silicon, carbon and oxygen content is given as atomic or molecular % of the total element content detected with XPS analysis). The hydrogen content cannot be measured using XPS analysis. Specification, Page 17, lines 3-8.

In example 1 of Vissing, a plasma polymer coating was formed from oxygen ( $O_2$ ) and hexamethyldisiloxane (HMDSO). However, the ratio of oxygen to HMDSO was so adjusted that the gas flow of HMDSO was approximately half as large as the gas flow of  $O_2$ . The plasma polymer layer had an oxygen content of 39.5 atomic %, a carbon content of 36.5 atomic % and a silicon content of 24 atomic % (see Vissing, column 5, table 1) with hydrogen not being detectable (see Vissing, column 2, line 56).

In Vissing's example 2, a plasma polymer coating was formed from oxygen ( $O_2$ ) and hexamethyldisiloxane (HMDSO). During this operation, the ratio of oxygen to HMDSO was varied in such a way that ultimately the gas flow of HMDSO was in a ratio of 27.5:100 to the gas flow of  $O_2$ . The plasma polymer layer has an oxygen content of 46.0 atomic %, a carbon content of 30 atomic % and a silicon content of 24 atomic % (see Vissing, column 5, table 1) with hydrogen not being detectable (see Vissing, column 2, line 56).

|                         | Feed Stream | Polymer               |                      |                      |                       |        |
|-------------------------|-------------|-----------------------|----------------------|----------------------|-----------------------|--------|
|                         |             | O <sub>2</sub> :HMDSO | Oxygen<br>(atomic %) | Carbon<br>(atomic %) | Silicon<br>(atomic %) | C:Si   |
| Specification,<br>Ex. 1 | 19:1        |                       | 39.4                 | 24                   | 36.6                  | 0.66:1 |
| Vissing, Ex. 1*         | 2:1         |                       | 39.5                 | 36.5                 | 24                    | 1.52:1 |
| Vissing, Ex. 2*         | 3.6:1       |                       | 46                   | 30                   | 24                    | 1.25:1 |

\* Data from Vissing, Col. 5, ln. 50- Col. 6, ln. 54

The plasma polymer layer of example 1 of the present application has been formed with a significantly larger oxygen concentration in the plasma gas than in Examples 1 and 2 of Vissing (19:1 compared with 2:1 and 3.6:1). This results in a reduced carbon content of the plasma polymer layer (0.66:1 compared with 1.52:1 and 1.25:1), thus rendering this layer more hydrophilic.

Furthermore, while the plasma polymer layers of Examples 1 and 2 of Vissing are characterized by a ratio of oxygen to silicon of 1.65:1 and 1.92:1, the ratio of carbon to silicon in the plasma polymer layer of Example 1 of the present application is 1.08. *Thus, while Vissing does disclose plasma polymerization using HMDSO and O<sub>2</sub>, Vissing does not disclose or suggest the claimed layered materials having a hydrophilic transport release layer with the claimed composition and properties.*

Additional Arguments

Terry (US 7,820,284) discloses (see claim 1) a microbe-resistant medical device comprising a substrate, a polymeric base coat applied to at least a portion of the substrate, at least one type of antimicrobial particle dispersed throughout the base coat; and a solid polymeric overcoat positioned over at least a portion of the base coat. The antimicrobial particles can be metals and metal salts, oxides and complexes (Terry, column 3, lines 59-60). The medical devices disclosed in Terry are either disposable or implantable (Terry, claim 20).

Terry specifically enumerates numerous options for the overcoats, none of which include any silicon, much less the claimed 20-60% silicon. While silicon generally produces hydrophobic polymers, Terry notes that nearly any hydrophilic polymer that can be dissolved in solvents can be used for the overcoat (Terry, column 4, lines 55-56). According to Terry (column 6, lines 36-41), the reasons for making the overcoat from a hydrophilic polymer are as follows: When hydrophilic polymers are used for the overcoat, the overcoated antimicrobial medical devices provide increased surface lubricity and decreased surface area (as compared to the base coat) of the medical device. Consequently, increased patient comfort, decreased tissue irritation, and increased antimicrobial effectiveness are achieved. Thus, according to Terry, the purposeful selection of a hydrophilic polymer provides useful benefits, which teaches away from the use of silicon.

Vissing (US 7,157,145) discloses (see claims 1 and 2) an article comprising a substrate and a plasma polymer coating comprising silicon, oxygen and carbon bonded to the surface of

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the substrate wherein the coating contains at least 22 and at most 27 atomic percent Si, at least 25 and at most 50 atomic percent O and at least 25 and at most 50 atomic percent C based on its total atomic number without hydrogen and/or fluorine. Vissing discloses (Column 4, lines 25-28) that the plasma polymer coating should be applied only to areas of substrate where "easy cleaning is important." In this regard, Vissing discloses (Column 4, lines 12-24) at least 25 articles, but fails to disclose a single article related to a medical devices, such as the coatings described in Terry.

The claimed layered material include a biocide layer having a biocidal active agent, and a transport control layer, having a particular composition, that covers the biocide layer. *Of particular interest, the transport control layer has a thickness and porosity adjusted to release an antimicrobial and non-cytotoxic quantity of the biocidal active agent out of the biocide layer and through the transport control layer.*

Terry explicitly requires that the overcoat provides controlled release of the antimicrobial agents (Terry, column 3, lines 25-26). The rate of release of an antimicrobial agent can be modified or controlled by selection of the polymers for the overcoat (Terry, column 6, lines 44-46 and 61-63), but Terry does not disclose or suggest any silicon containing polymers. The overcoat polymer is permeable or semi-permeable to the agent(s) released from the antimicrobial particles (Terry, column 5, lines 10-14).

*In contrast, Vissing does not disclose or suggest that the plasma polymer layers of Vissing could meet these permeability requirements. In fact, Vissing does not provide any information regarding porosity or permeability of the plasma polymer layers. Indeed the skilled person would not expect that a plasma polymer layer that is optimized for the purpose of easy cleaning (Vissing; column 1, lines 57-58; column 2, lines 35-36) would also meet the requirement of permeability for an antimicrobial agent.*

Thus, the following argument of the Office Action (paragraph 21, page 7) is clearly the result of an improper *ex-post facto* approach where the claims were used as a roadmap for the rejection:

“With respect to the requirement that the transport control layer has a gas permeability for oxygen which is preferably in the range from 500 to 700 ( $\text{cm}^3 \text{ bar}/(\text{day m}^2)$ ), this is a property of the polymer having the instantly claimed silicon, oxygen and carbon content. As Vissing teaches a polymer which has silicon, oxygen and carbon content within the range of the instantly claimed (and specifically hexamethyldisiloxane- which is exemplified in Applicants' own specification, too) it'd be expected that it too would have overlapping  $\text{O}_2$  permeability. Therefore, modification of the medical device of Terry to substitute the hydrophilic polymer outercoat layer with the easy-to-clean plasma polymer layer of Vissing would have been *prima facie* obvious, and the resulting medical product reads on the medical product of instant claims 36-42, 45 and 46.”

In contrast to these assertions, a person of skill in the art relying on Vissing's disclosure could neither know nor expect that the plasma polymer layers disclosed by Vissing could have the desired permeability. For this reason, the skilled person would have no reason to expect that the polymer overcoat of Terry could be replaced by a plasma polymer layer of Vissing without detrimental effects on the permeability. *Thus, it was not until the present invention was made (i.e., a plasma polymer layer similar to that of Vissing was indeed used as transport control layer for a biocide-containing layer) that the skilled person had the chance to recognize that such plasma polymer layers could provide the desired permeability.* Applicant reiterates that the pending claims require “a biocide layer having a biocidal active agent, and . . . a transport control layer covering the biocide layer, having a thickness and porosity *adjusted to release an antimicrobial and non-cytotoxic quantity of the biocidal active agent out of the biocide layer and through the transport control layer* (see, also, claims 37 & 38).

Furthermore, the plasma polymer coatings produced by Vissing (column 3, lines 59-62) are generally hydrophobic. In particular, Vissing discloses that the plasma polymer coating preferably has an angle of contact with water of  $>90^\circ$ , preferably  $>95^\circ$ , and more preferentially  $>100^\circ$ . Accordingly, the plasma polymer coating is preferably hydrophobic, whereas the over coat of Terry is preferably hydrophilic. In addition, Terry expressly noted that using a hydrophilic overcoat was critical in order to provide increased patient comfort, decreased tissue irritation, and increased antimicrobial effectiveness are achieved. *A person of skill in the art would clearly understand that*

*these benefits for a medical device greatly outweigh the self-cleaning benefits of Vissing and would not substitute the overcoat of Terry with the self-cleaning coating of Vissing as suggested by the Office Action.*

*For at least this reason, in contrast to the hindsight reconstruction relied upon in the Office Action, a skilled person would not modify the device of Terry to replace the hydrophilic polymer overcoat with the plasma polymer layer of Vissing.* In particular, Terry and Vissing provide directly contradictory teachings regarding hydrophilicity and hydrophobicity. Terry unambiguously prescribes making the overcoat from a hydrophilic polymer while Vissing specifically directs the skilled person to hydrophobic layers. Thus, a person skilled in the art would understand that this is because the over coat of Terry and the self-cleaning coating of Vissing are for completely different purposes and would not substitute one for the other.

Terry lists benefits which arise from the selection of a hydrophilic polymer – in particular, increased patient comfort, decreased tissue irritation, and increased antimicrobial effectiveness are achieved. A person skilled in the art would not readily compromise all these benefits for an easier cleaning of the surface. Particularly for the disposable or implantable medical devices disclosed in Terry, where self-cleaning would not be seen as a benefit. Thus, due to the loss of all the benefits which are related to hydrophilic polymers of Terry, the replacement of the hydrophilic polymer by the plasma polymer of Vissing cannot be considered as an “improvement” as alleged in the Office Action (page 5, item 13, last sentence).

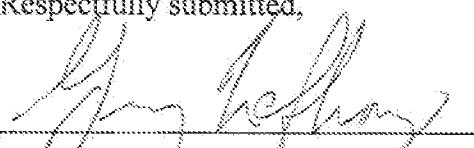
In summary, while Terry requires specific permeability parameters for controlled release coatings, Vissing provides no information regarding permeability of the plasma polymer coatings disclosed therein. Furthermore, while Terry relates to hydrophilic coatings, Vissing relates to hydrophobic coatings. Thus, there is no motivation or suggestion to combine Terry and Vissing. Furthermore, because Vissing provides no disclosure regarding permeability, there would be no reasonable expectation of success absent improper hindsight reconstruction of the pending claims. For at least for these reasons, the subject matter of claims 36-42, 45, 46 and 48

is not obvious over Terry in view of Vissing. As Burrell does not correct the deficiencies identified above, the subject matter of claim 44 is not obvious over Terry in view of Vissing and Burrell. These arguments are even stronger for the dependent claims, including dependent claims 37, 38 and 48. Accordingly, Applicant respectfully requests that all rejections based on the cited art be withdrawn.

**Conclusion**

For at least the reasons set forth above, the independent claims are believed to be allowable. In addition, the dependent claims are believed to be allowable due to their dependence on an allowable base claim and for further features recited therein. The application is believed to be in condition for immediate allowance. If any issues remain outstanding, Applicant invites the Examiner to call the undersigned Greg Lefkowitz (direct line 561-962-2110) if it is believed that a telephone interview would expedite the prosecution of the application to an allowance.

Respectfully submitted,

  
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